

Effectiveness and Safety of Thoracic Epidural Analgesia in Liver Resection Surgery

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ABSTRACT

Objective: To study the effectiveness and complications of thoracic epidural analgesia in patients undergoing open liver resection surgery

Study Design: Prospective Observational Study.

Place and Duration of Study: Army Liver Transplant Unit, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Aug 19 to May 22.

Methodology: A total of 50 patients who had open liver resection surgery and received thoracic epidural analgesia for pain relief were included in the study. All patients were above 18 years of age. Patients who had abnormal coagulation were excluded from the study. The effectiveness of the epidural was assessed by measuring the numerical rating scale (NRS) in the post-operative period. Complications, including accidental removal and epidural haematoma, were noted.

Results: 48(96%) group subjects had adequate pain relief with no to mild pain in 7(13.7%), 15(29.4%), 38(74.5%) and 41(80.4%) patients on the 1st, 2nd, 3rd, and 4th post-operative day (POD), respectively, with a *p*-value <0.001. The frequency of moderate pain was recorded in 18(35.3%) patients in the first POD, 24(47.1%) patients in the second POD, 7(13.7%) patients in the third POD, and 9(17.60%) on fourth POD. The frequency of pain was severe in 25(49.0%),

Conclusion: Thoracic epidural analgesia is an efficient and safe modality of analgesia after liver resection.

Keywords: Analgesia, Hepatic Resection, Post-operative Pain, Thoracic Epidural.

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INTRODUCTION

Hepatic resection is considered a major abdominal surgery. Common indications are: benign and malignant primary hepato-biliary tumours, colorectal hepatic metastasis, donation for liver transplantation, and liver trauma.¹ Liver resection is performed by a right subcostal incision or a reverse L-shaped incision. Irrespective of the type of incision, hepatic resection is associated with significant post-operative pain.² Different centres use different modalities of analgesia, which include thoracic epidural analgesia, patient-controlled analgesia (PCA), intravenous opioids (boluses or infusion), local wound infiltration, and bilateral subcostal TAP block.³ Although there is concern regarding the safety of thoracic epidural in coagulopathy, it is often used in liver resection to provide high-quality analgesia.⁴ It is used as part of a multi-modal regime in enhanced recovery programmes after liver resection. Intraoperatively, a thoracic epidural helps to decrease surgical stress response, lower anaesthetic requirements, maintain a low central venous pressure,

and decrease blood loss.⁵ Postoperatively, it helps in providing pain relief, early mobilization, and decreasing post-operative pulmonary and cardiac complications.⁶ Potential risks and complications associated with epidural, such as haematoma, abscess, and spinal cord damage, raise suspicion regarding its use in liver surgery, where coagulopathy and decreased immunity are known hazards.⁷ Another frequently occurring problem is failure of procedure or suboptimal performance (20-30%), resulting in poor pain management. Even if a patient has normal coagulation before surgery, coagulation disorders frequently occur postoperatively, which can lead to complications, especially during epidural catheter removal. Removal of the catheter, whether accidental or intentional, may cause an epidural hematoma. Because of the above-mentioned factors, there is controversy regarding its safety in these patients.⁸

Therefore, the rationale of our study is to study its safety in our population. The primary outcome of this study was to assess the quality of analgesia by measuring the post-operative numerical rating score (NRS). The secondary outcome was the evaluation of the safety of thoracic epidural analgesia in terms of the incidence of catheter-related complications.

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METHODOLOGY

After approval from the Hospital Ethics Committee (IERB # A/28/EC/465/2022), this study was conducted at the Army Liver Transplant Centre of the Pak Emirates Military Hospital, Rawalpindi, Pakistan, from Aug 2019 to May 2022. Written informed consent was obtained from 50 patients who were booked for hepatic resection for this prospective review. The sample size was calculated with the help of the WHO sample size calculator, keeping confidence level(1- α) to be 95%, anticipated population proportion (P) to be 0.4, absolute precision (d) required to be 0.1, relative precision(ϵ) to be 0.25, and estimated population size (N) to be 100. The sample came out to be 49. Non-probability consecutive sampling was done to enroll 50 participants for the study.

Inclusion Criteria: Patients aged > 18 years planned for open liver resection with international normalized ratio <1.5 and platelet count > 100 were included in the study.

Exclusion Criteria: Patients with age <18, coagulopathy (INR>1.5), and thrombocytopenia (platelet count <100) were excluded from the study.

A thoracic epidural was performed by consultant anaesthetists who had experience and good dexterity. Patients were evaluated thoroughly in the pre-anaesthesia clinic. They were anaesthetised by using a standard anaesthetic technique. Induction was performed by using Midazolam 2mg, Morphine 10mg, and Propofol 2mg/kg. Muscle relaxation was accomplished by using Atracurium 0.5mg/kg and then the trachea was intubated. An arterial line was navigated in the left radial artery, and a central venous pressure line was secured in the right jugular vein using ultrasound guidance. Patients were then placed in lateral position and thoracic epidural was performed at T 6-7, T 7-8 or T 8-9 level. The epidural space was marked and accessed with the help of a Tuohy needle (18G). An epidural catheter was inserted 5 cm deep into the epidural space with the help of the loss-of-resistance technique. A test dose of 3 ml 0.5% Bupivacaine with adrenaline 1:200000 was done. A 10ml loading dose of 0.125% Bupivacaine was then given in 5 ml increments. Intraoperative analgesia was provided by an infusion of Bupivacaine at a rate of 10ml/hour at a dose of 0.125%. Intraoperatively, CVP was maintained at 2-5 cm H₂O by fluid restriction and a slight head-up position. Arterial blood gases were measured 1-hourly for correction of electrolytes and

acid-base status. Haemoglobin was maintained above 9gm/dl. After hepatectomy, patients were given intravenous fluids to achieve normovolemic status and a CVP of 7-8 cm H₂O. At the end of surgery, patients were extubated in the theatre and shifted to the ICU. Epidural infusion was continued for the next 4 days at a rate of 10 ml/hour. Paracetamol (1 gm, 8 hourly) was given intravenously. The maximum Numerical Rating Score (NRS) for pain was measured in the first 12 hours postoperatively on the 1st, 2nd, 3rd, and 4th postoperative days. Baseline investigations, including platelet count and INR, were performed daily and recorded for the 1st, 2nd, 3rd, and 4th post-operative days. Any incidence of nausea, vomiting, pruritus, headache, or sensory or motor deficit was also noted. The epidural catheter was removed on the 4th postoperative day, provided that the INR was less than 1.5 and platelet count was greater than 100x10⁹/L, and after a 12-hour interval from the last Enoxaparin. The frequency of pain was recorded on the 1st, 2nd, 3rd, and 4th post-operative days, and it was the primary outcome variable.

Statistical analysis was performed using the statistical package of social science (SPSS) version 26. Mean $\pm$ SD were computed for quantitative variables like age, weight, numerical rating score (NRS), International Normalized Ratio (INR) and platelet count. Frequency and percentages were calculated for qualitative variables like gender, Child-Pugh class and type of surgery. Chi square test (for qualitative variables) and ANOVA (for quantitative data) were applied. The p value $\leq$ 0.05 was considered significant.

RESULTS

Out of 50 patients included in the study, 32(64%) were male and 18(36%) were female. 46(92%) patients were in Child-Pugh Class A and remaining 18(36%) were in Child-Pugh Class B of liver disease. 35(70%) patients underwent major hepatic resection (3 or greater than 3 segments), and 11(22%) underwent minor hepatic resection (resection of <3 segments). The descriptive statistics of demographics are presented in Table-I.

Table-I: Descriptive Statistics of Demographic Variables (n=50)

Parameter		Mean $\pm$ SD (n=50)
Age(Years)		55.94 $\pm$ 8.599
Weight(Kg)		74.86 $\pm$ 9.49
		Frequency (%)
Gender	Male	32(64)
	Female	18(36)
Child-Pugh Class	A	46(92)
	B	4(8)
Type Of Surgery	Major Hepatectomy	39(78)
	Minor Hepatectomy	11(22)

48(96%) group subjects had adequate pain relief with no to mild pain in 7(13.7%), 15(29.4%), 38(74.5%), and 41(80.4%) patients on the 1st, 2nd, 3rd, and 4th post-operative day (POD), respectively, with a p -value <0.001 as shown in Table-II. The frequency of moderate pain was recorded in 18(35.3%) patients in the first POD, 24(47.1%) patients in the second POD, 7(13.7%) patients in the third POD, and 9(17.60%) on fourth POD. The frequency of pain was severe in 25(49.0%).

Table-II: Frequency of pain post-operatively (n=50)

Post-Op Day	Mild Pain (NRS 0-3) Frequency (%)	Moderate Pain (NRS 4-6) Frequency (%)	Severe Pain (NRS 7-10) Frequency (%)	p -value
1st	7(13.7)	18(35.3)	25(49.0)	
2nd	15(29.4)	24(47.1)	11(21.6)	<0.001
3rd	38(74.5)	7(13.7)	5(9.8)	<0.001
4th	41(80.4)	9(17.6)	1(2.0)	<0.341

The international normalized ratio was 1.32 ± 0.135 , 1.220 ± 0.118 , 1.15 ± 0.103 , and 1.07 ± 0.064 on the first, second, third, and fourth post-operative days. The INR peaked on postoperative day two with a mean of 1.220 ± 0.118 and became normal in patients by the 4th post-operative day with a mean of 1.07 ± 0.064 . The platelet count remained within normal limits on 1st, 2nd, 3rd, and 4th post-operative days with a mean platelet count of 136.22 ± 43.68 , 140.06 ± 45.36 , 143.36 ± 42.96 , and $145.78 \pm 44.62 \times 10^9$ per litre, respectively, as presented in Table-III. Catheters were left in place for 3.98 ± 0.141 days. There were 2(4%) accidental dislodgements of the catheter, while 48(96%) epidural catheters were successful with adequate analgesia. The patients with dislodged catheters were shifted to patient-controlled analgesia with morphine. There was no incidence of hematoma formation or pruritus. (Table-IV).

Table-III: International Normalized Ratio (INR) & Platelet Count Post-Operatively (n=50)

	1st Post-Op Day	2nd Post-Op Day	3rd Post-Op Day	4th Post-Op Day	p -value
International Normalized Ratio	1.32 ± 0.13	1.22 ± 0.11	1.15 ± 0.10	1.07 ± 0.06	<0.001
Platelet Count ($\times 10^9$ PER LITRE)	136.22 ± 43.68	140.06 ± 45.36	143.36 ± 42.96	145.78 ± 44.62	<0.001

Table-IV: Frequency of Different Complications (n=50)

Complication	Frequency (%)	
	Yes	No
Dislodgement	2(4)	48(96)
Post-operative Nausea Vomiting (PONV)	5(10)	45(90)
Hypotension	2(4)	48(96)

DISCUSSION

The study demonstrated that thoracic epidural analgesia is an effective and safe modality for

postoperative pain management following open liver surgery, with an acceptable rate of associated complications. The frequency of pain was monitored for 4 postoperative days, in relation to the type of surgery. 78% of the subjects underwent major hepatectomy, of whom 49% experienced severe pain postoperatively.

Epidural analgesia was a successful and safe choice for our patients. It blunted the peri-operative neuro-endocrine stress response and provided opioid free postoperative analgesia.⁹ Epidural has been considered an important part of the enhanced recovery after surgery (ERAS) protocol for major abdominal surgeries. It offers a lot of benefits when compared with general anaesthesia.¹⁰ It has immune-protective effects because it attenuates neuroendocrine stress response and immunosuppression by preserving the cytotoxic properties of helper and natural killer T cells postoperatively. In addition, epidural anaesthesia lessens postoperative pulmonary complications as the patient can perform effective incentive spirometry and deep breathing exercises. Pain can have adverse outcomes in terms of post-operative pulmonary dysfunction by affecting diaphragmatic excursion. The decrease in FRC results in atelectasis and pneumonia.¹² The use of epidural analgesics prevents this vicious cascade by improving lung functions and improving pulmonary outcome in patients of hepatic resection with large incisions. Atalan *et al.*, found in their study that liver transplant donors who were given an epidural did not develop post-operative pulmonary difficulties, had a fast-track recovery, and had a limited duration of stay in hospital.¹³ Data regarding procedure-related and immediate complications associated with epidural analgesia were reported for simplicity.

Continuous epidural infusion spares opioids required in the first forty-eight hours of surgery, which facilitates early gut motility and mobilization. The quick ambulation in post-operative patients also averts cardiac and thromboembolic complications. There are studies similar to Bell *et al.*, in which epidural analgesia has been reported to be inadequate, patchy, and associated with accidental dislodgement.¹⁴ However, in our study, the incidence of accidental dislodgement was very low, that is, 2%. No epidural was found to be ineffective or patchy, which is quite reassuring.

There is a well-established role in maintaining a low CVP during liver resection for the prevention of

blood loss and reduction of transfusion requirements.¹⁰ Balanced general anaesthesia, vasodilatation caused by thoracic epidural blockade, and restrictive fluid therapy are useful for maintaining low CVP during hepatic transection. Thus, epidural analgesia offers a lot of benefit in hepatectomies by lowering CVP and reducing surgical blood loss.¹¹ Therefore, we have to carefully weigh risks against benefits.

Coagulopathy is one of the common problems after hepatic resection, which is a manifestation of altered liver synthetic function. It is also attributed to prolonged surgery, application of occlusion techniques, blood loss, and the magnitude of resected liver tissue.¹⁵ There are many patients whose coagulation profiles and liver functions are within normal limits as donors. An accurately functioning epidural catheter, when used properly, provides superior analgesia in comparison to patient-controlled analgesia (PCA). In a prospective randomized trial conducted by De Gasperi *et al.*, epidural analgesia proved a superior alternative to intravenous PCA in open liver surgery.¹⁶ Although patient-controlled analgesia (PCA) using opioids is an effective and popular modality of providing pain relief after surgery, opioids have been found ineffective for pain that is associated with movement, and they come with a price of potential side effects like sedation, respiratory depression, nausea, vomiting, pruritus, constipation, urinary retention, all of which are detours from the road of recovery. Plianngarn *et al.*, reviewed randomized controlled trials comparing the effectiveness of epidural analgesia to PCA in patients undergoing open liver resection. They found epidural analgesia to be superior to PCA for pain control, but there was no significant difference in blood transfusion requirements, length of hospital stay, and complications.¹⁷ They reported data for 48hrs post-operative period, but we recorded the pain scores 96 hours post-operatively.

Jennifer *et al.*, performed a retrospective review of the safety of thoracic epidural in open liver resection patients. They found that coagulopathy was as frequent as 53 percent after liver resection. They established that epidural analgesia was safe for minor liver resections, but safety for major resections was uncertain.¹⁸ In our study, there were more (39%) major resections and fewer (11%) minor resections, but there was no coagulopathy (INR >1.5) or hematoma formation in any patient.

LIMITATION OF STUDY

This study had two main limitations. First, it was observational in design and did not include randomisation or a control group. Second, the assessment was limited to immediate postoperative complications; therefore, delayed catheter-related complications and longer-term outcomes were not evaluated.

CONCLUSION

Thoracic epidural analgesia was found to be an effective modality for postoperative pain relief following open liver surgery. It provided progressive improvement in pain control over the first four postoperative days, supporting early recovery and patient comfort. The technique was associated with an acceptable complication profile, with only a small number of catheter-related events observed. No serious complications, such as epidural haematoma or neurological deficit, were reported in this study. These findings suggest that, with careful patient selection and coagulation monitoring, thoracic epidural analgesia can be used safely and effectively after open hepatic resection.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AR & KM: Data acquisition, data analysis, critical review, approval of the final version to be published.

AMR & UEM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MSK & AK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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